Journal of the American College of Cardiology Vol. 59, No. 17, 2012

Published by Elsevier Inc.
ISSN 0735-1097/$36.00
doi:10.1016/j.jacc.2012.02.011

EDITORIAL COMMENT

How to Supplement Endpoints of Ventricular Tachycardia Ablation

Is There a Role for Noninvasive Programmed Ventricular Stimulation?*

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Endpoints for interventional procedures such as catheter ablation should be clearly defined, reproducible, practicable to measure, and widely accepted. In addition, good endpoints should have significant predictive impact on long-term outcome (e.g., the recurrence of tachycardia after successful catheter ablation procedures). By that, they are not only markers of treatment quality for the individual patient but also of utmost scientific value because they allow the solid comparison of different treatment technologies or treatment strategies. In the field of catheter ablation, we have the privilege of having such endpoints for most of the procedures being performed: complete accessory pathway block in patients with Wolff-Parkinson-White syndrome syndrome or bidirectional isthmus block in patients with typical atrial flutter predict a very low risk for arrhythmia recurrence during long-term follow-up. Even in patients with complex arrhythmias such as paroxysmal atrial fibrillation, the endpoint of complete pulmonary vein isolation is well defined and generally accepted. In the setting of catheter ablation of ventricular tachycardia (VT) in patients with organic heart disease, however, procedural endpoints are less well defined. The most widely accepted endpoint is noninducibility of VT by programmed ventricular stimulation assessed at the end of the ablation procedure (1,2). Definition of noninducibility may relate to the clinical tachycardia, to VT of certain cycle lengths (e.g., only those with a cycle length equal to or longer than the clinical tachycardia), or even to any inducible VT. Unfortunately, no standards for the stimulation protocol pre-ablation and post-ablation (e.g., number of extrastimuli applied, basic drive cycle length, number of stimulation sites) are generally accepted. In addition, execution of endpoint assessment by using programmed stimulation at the end of an ablation procedure is sometimes limited by the unstable medical conditions of the patients being treated. Moreover, completion of a full programmed stimulation protocol after hours of VT ablation may require some discipline, which at times is difficult to deliver.

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The best conditions to apply programmed stimulation are found in patients with remote myocardial infarction and the following: 1) 12-lead electrocardiogram documentation of the clinical tachycardia; 2) reproducible inducibility of the clinical tachycardia; and 3) no inducibility of other nonclinical tachycardias. Delineation of areas critical for the maintenance of the tachycardia by means of voltage- and pace-mapping and/or activation- and entrainment-mapping often allows the creation and delivery of an effective ablation strategy, which terminates the tachycardia and renders the patient noninducible. However, in clinical practice, this situation is rare. Frequently, ablation sessions are complicated by the inducibility of multiple VT morphologies and/or fast and hemodynamic instable tachycardias requiring repetitive electrical defibrillation (1,2). In addition, precise identification of a clinical tachycardia may be difficult in patients without 12-lead electrocardiogram documentation. In the setting of incessant VT or electrical storm, it is also almost impossible to assess the complete preablation inducibility due to the critical clinical situation. During the ablation session, factors such as sedation or general anesthesia, other pharmacological interventions, changes in autonomic tone, transient ischemia, or hemodynamic deterioration may also have an influence on the reproducibility of tachycardia induction. With these limitations in mind, what is the value and relevance of programmed stimulation as an endpoint for the procedure and as a useful tool for risk assessment for VT recurrence?

Early single-center studies in patients with post-myocardial VT undergoing catheter ablation indicated some value of programmed stimulation to predict the risk for tachycardia recurrence during mid-term follow-up (3–5). These studies found that patients rendered completely noninducible by the ablation procedure were at significantly lower risk for the recurrence of clinical and nonclinical VT during follow-up. However, even the noninducible patients still had a considerable risk of VT recurrence of approximately 20% to 30% during the first year after ablation. In most of the more recent larger-scale, single-center and multicenter studies, no significant predictive value of programmed stimulation performed at the end of the ablation procedure was observed for VT recurrence during follow-up (6–9). In these studies, other markers were identified to predict VT recurrence such as number of inducible tachy-

*Editorials published in the *Journal of the American College of Cardiology* reflect the views of the authors and do not necessarily represent the views of *JACC* or the American College of Cardiology.

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cardias before ablation, left ventricular end-diastolic diameter, presence of incessant VT, or advanced heart failure. These divergent results may be in part due to the changes in patient population undergoing catheter ablation more than 10 years ago compared with more recent studies. Indeed, the widespread use of thrombolysis and/or immediate coronary intervention, which have become standard for the treatment of acute myocardial infarction, have changed the substrate of VT and the response to programmed stimulation (10).

In this issue of the *Journal*, Frankel et al. (11) report the results of an interesting study in which programmed ventricular stimulation was performed noninvasively days after a VT ablation procedure via implanted implantable cardioverter-defibrillator devices (noninvasive programmed ventricular stimulation [NIPS]) in addition to acute postablation stimulation to improve prediction of VT recurrence. More than two-thirds of the patients investigated had ischemic VT and approximately one-third had nonischemic VT. Only 11 of 167 patients who underwent direct postablation programmed stimulation had inducible clinical VT (7%). These patients did not undergo NIPS, unfortunately; it would have been interesting to see reproducibility of clinical VT induction at NIPS. After excluding an additional 46 patients (mainly for clinical reasons) and 11 patients with spontaneous recurrence of clinical VT, a total of 132 patients finally underwent NIPS approximately 3 days after the ablation procedure. Twenty-four of 132 patients had inducible clinical VT (18%), 49 patients had inducible nonclinical VT (37%), and 59 patients (45%) were not inducible. The main finding of the study is that a relatively high percentage of patients being noninducible at the end of the ablation session have inducible clinical VT just a few days after the procedure. This finding may be explained by the lack of durability of radiofrequency-induced ventricular lesions potentially allowing re-conduction through critical VT isthmus sites effectively blocked during the ablation session.

The results of the study by Frankel et al. (11) provide additional evidence that re-conduction may play a significant role for the recurrence of VT, similar to what has been shown in patients undergoing catheter ablation for atrial fibrillation. In addition, the cofactors for the limited predictive strength of programmed stimulation at the end of the ablation session defined here (e.g., general anesthesia, pharmacological intervention) may have at least in part been overcome by performing programmed stimulation at a later stage. Although not powered as a mortality study, it is striking to recognize the high 1-year mortality rates observed in patients with inducible clinical VT (21%) and inducible nonclinical VT (23%) at NIPS versus only 3% in noninducible patients. However, the details on the mode of death in these patients were not reported. Sadly, according to Figure 2 of the paper (11) and unfortunately not explained by the authors in detail, the recurrence rate of any VT in NIPS-negative patients at 400 days of follow-up still was close to 20%.

The most striking limitation of NIPS is that this strategy is not very helpful as an endpoint for catheter ablation of VT. The procedure occurred days before re-assessment and potential validation of the intervention outcome. What to do with "NIPS-positive" patients? Possibilities include early re-ablation, intense and careful follow-up, or addition of antiarrhythmic drugs. Nevertheless, progress to improve outcome of patients with recurrent VT undergoing catheter ablation slowly evolves, and the important new data provided by the study from Frankel et al. (11) represent such a step. However, additional studies are clearly necessary to further delineate the role of NIPS to better understand the prediction of VT recurrence after catheter ablation and to improve the management and outcome of such patients. As a word of caution: in the past, programmed stimulation has failed many times to predict efficacy of antiarrhythmic drugs, to identify candidates for implantable cardioverter-defibrillator implantation, and to identify patients with high risk for sudden cardiac death (12). Hopefully, history will not repeat with NIPS.

Are there alternatives on the horizon for endpoints better than those generated by programmed stimulation for the prediction of risk for recurrence of VT after catheter ablation? Nothing that is clearly visible at this point in time. New treatment strategies such as combined endo- and epicardial ablation or the (complete?) ablation of late ventricular activation (so-called LAVA ablation) are currently under intense clinical investigation. Whether these aggressive ablation strategies lead to overtreatment or improve the outcome of patients undergoing catheter ablation of VT in the presence of structural heart disease needs to be shown in the studies to come. As long as we do not have convincing studies presenting better endpoints, we should continue to use noninducibility as the endpoint of VT catheter ablation—potentially supported by NIPS.

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Key Words: catheter ablation ■ programmed stimulation ■ ventricular tachycardia.